Claims 1-4 and 21 stand rejected under 35 U.S.C. 102(a) as being anticipated by Tempest, et al.

Claims 1-4, 6, 7, and 21 stand rejected under 35 U.S.C. 103 as being unpatentable over Tempest, et al. in view of Beeler, et al.

Claims 1-4, 6, 7, and 21 stand rejected under 35 U.S.C. 103 as being unpatentable over Jones, et al. in view of Beeler, et al.

These rejections are respectfully traversed.

The present invention is one aspect, as defined in Claim 1, is directed to a human-murine antibody against respiratory syncytial virus. The antibody comprises a human antibody containing at least one CDR from each of the variable heavy and variable light chains of a murine monoclonal antibody against respiratory syncytial virus.

In another aspect, as defined in Claim 21, there is provided an antibody against respiratory syncytial virus which comprises a human constant region, a heavy chain and light chain variable region, each of which comprises a framework region, at least a portion of which is human, and three complementary determining regions. Each complementary determining region is derived from a murine monoclonal antibody.

With respect to the Tempest reference, Applicant, in parent Application Serial No. 08/290,592, now U.S. Patent No. 5,824,307, submitted a Declaration Under 37 CFR1.131 of Leslie S. Johnson. In such Declaration, Applicant stated that Applicant conceived the present invention prior to March 1991, the effective date of the Tempest reference, and from such conception, diligently worked to reduce the invention to practice.

Applicants note that the Examiner states that Exhibit 1 in support of the Rule 131 Declaration states that "murine CDRs will be substituted into human heavy and light

chain CDNA's". Claim 1 states that the human-murine antibody has at least one CDR from each of the variable heavy and variable light chains of a murine monoclonal antibody. Claim 1 clearly falls within the scope of the invention conceived in Exhibit 1.

Claim 21, which defines a heavy chain variable region and a light chain variable region, each of which include three complementarity determining regions, each derived from a murine monoclonal antibody, also is within the scope of the invention conceived in Exhibit 1. Thus, Exhibit 1 supports the conception of the claimed invention. In addition, Applicant submits with this response copies of Exhibits 2, 3, and 4, which previously were omitted inadvertently. Exhibits 2, 3, and 4 demonstrate the reduction to practice of the claimed invention. Therefore, Tempest no longer is an effective reference against the above-identified application under 35 U.S.C. 102(a) or 35 U.S.C. 103.

Beeler discloses only murine monoclonal antibodies. It does not disclose or even remotely suggest to one of ordinary skill in the art human-murine antibodies. Furthermore, Beeler does not disclose or even remotely suggest to one of ordinary skill in the art humanized antibodies of any sort. Especially, Beeler does not disclose or suggest to one of ordinary skill in the art which, if any murine monoclonal anti-RSV antibodies could be humanized and retain vital neutralization properties at therapeutically effective levels.

In view of the above, the human-murine antibodies of the invention are patentable over Beeler.

Regarding the Jones reference, Jones does not disclose or even remotely suggest to one of ordinary skill in the art the use of CDRs with specificity to any RSV antigen. Jones did not use the CDRs from both the variable heavy and variable light

chains. In Jones, only a mouse V_h CDR was grafted into a human heavy chain framework region. Furthermore, Jones only examined antigen binding, comparing the binding of the mouse monoclonal and polyclonal MVnp anti-idiotypic antibodies. The difference in affinity to the anti-idiotypic antibody only shows that the CDR has lost certain determinants in the humanized antibody. Also, Jones provides no suggestion that the antibodies of Jones are useful for use in human therapy. Jones, therefore, does not render Applicant's claimed antibodies obvious to one of ordinary skill in the art.

Jones and Beeler, therefore, alone or in combination, do not disclose or even remotely suggest Applicant's claimed human-murine antibodies to one of ordinary skill in the art, and thus do not render Applicant's claimed human-murine antibodies obvious to one of ordinary skill in the art. It is therefore respectfully requested that the rejections under 35 U.S.C. 103 be reconsidered and withdrawn.

Claims 1-4, 6, 7 and 21 stand rejected under 35U.S.C. 103 as being unpatentable over Queen, et al. in view of Beeler, et al. This rejection is respectfully traversed.

Queen discloses a humazied antibody which has complementarity determining regions, or CDRs, from a donor immunglobulin, which may, for example, be a mouse or rat immunoglobulin, and heavy and light chain variable region frameworks from human accepto immunoglobulin heavy and light chain frameworks. The antibody may be an anti-Interleukin-2 receptor antibody, an anti-Herpes Simplex Virus (HSV) antibody, an anti-CD33 antibody, an anti-Cytomegalovirus (CMV) antibody, an anti-Interferon-gamma antibody, or an anti-Tac antibody. Queen, however, does not disclose or even remotely suggest to one of ordinary skill in the art a human-murine antibody against respiratory syncytial virus which comprises a human antibody containing at least one CDR from

each of the variable heavy and variable light chains of a murine monocloral antibody against respiratory syncytial virus.

Beeler, as stated hereinabove, discloses only marine monocloral antibodies. Thus, Beeler adds nothing to the disclosure of Queen and therefore the combination of Queen and Beeler does not even remotely suggest applicant's claimed antibody against respiratory syncytial virus obvious to one of ordinary skill in the art. It is therefore respectfully requested that the rejection under 35 U.S.C. 103 be reconsidered and withdrawn.

Claims 2-4, 6, 7, and 21 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to convey reasonably to one skilled in the art that the inventor, at the time the application was filed, had possession of the claimed invention. This rejection is respectfully traversed.

The Examiner has taken the position that the specification does not support the limitations "comprises a framework region, at least a portion of which is human" in Claim 21.

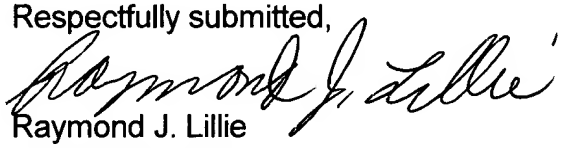
Support for such limitation is found in the examples, and at Page 5 lines 14-23. Therefore, Claim 21, which is supported by the specification, complies with the requirements of 35 U.S.C. 112, first paragraph, and it is therefore respectfully requested that the rejection under 35 U.S.C. 112, first paragraph, be reconsidered and withdrawn.

Regarding the rejection under 35 U.S.C. 112, second paragraph, one skilled in the art would understand that the light and heavy chain constant regions denied in Claim 21 are human, and that Claim 21 defines an antibody in which each of the three complementary determining regions of both the heavy and light chain variable regions are of murine origin. Support is found in the specification at Page 5, lines 6-23 and 30-33. It is

therefore respectfully requested that the rejection under 35 U.S.C. 112, second paragraph, be reconsidered and withdrawn.

For the above reasons and others, this application is in condition for allowance, and it is therefore respectfully requested that the rejections be reconsidered and withdrawn and a favorable action is hereby solicited.

Respectfully submitted,



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